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EXAMINER
HUYNH, PHUONG N

ART UNIT	PAPER NUMBER
1644	10

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/787,494	Applicant(s) HARRIS ET AL.	
	Examiner " Neon" Phuong Huynh	Art Unit 1644	

-- The MAILING DATE of this communication appears on th cover she t with the corr spond nce address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 November 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-58* is/are pending in the application.

4a) Of the above claim(s) *11 and 13-58* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10 and 12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 1-58 are pending.

2. Applicant's election with traverse of Group III, Claims 1-10 and 12 drawn to a composition comprising a recombinant β human chorionic gonadotropin fusion protein wherein the recombinant fusion protein consisting of βhCG protein, fragment or analog joined to a β-galactosidase protein of SEQ ID NO: 2 or fragment thereof, chitosan-based adjuvant, filed 11/12/02, is acknowledged. The traversal is on the grounds that (1) both SEQ ID NO: 2 and SEQ ID NO: 4 define the amino acid sequence of a fusion protein comprising a fragment of βhCG (amino acids 22-165) linked to a β-gal fragment while SEQ ID NO: 4 is a fusion protein comprising a fragment of βhCG (amino acids 22-165) linked to the FLAG peptide, (2) claims 1-58 are directed to a genus of βhCG wherein the species of βhCG such as the ones are listed on page 3, and (3) while the Examiner asserts that Partain teaches βhCG and a chitosan-based adjuvant (species 1), the Partain does not teach a βhCG fusion protein and a chitosan-based adjuvant (species 4-6). This is not found persuasive because of the reasons set forth in the restriction mailed 7/2/02. Claim 1 recites a composition comprising βhCG and/**or** fusions, fragments or analogs thereof and a chitosan-based adjuvant. The EP0368,253 patent (of record, Partain et al, May 1990, PTO 1449) teaches a composition of instant claim 1 comprising β human chorionic gonadotropin protein (βhCG) (see column 10, lines 37-39, in particular) and chitosan-based adjuvant (See column 2, lines 32-37, column 9, lines 28-37 and column 9, lines 37-43), which is a species 1 as defined by applicant on page 3 of the election. Since Applicant's inventions do not contribute a special technical feature when viewed over the prior art they do not have single general inventive concept and lack unity of invention. Accordingly, Groups I-XVIII are not so linked as to form a single general inventive concept and restriction is proper. In response to applicants' argument that both SEQ ID NO: 2 and SEQ ID NO: 4 define the amino acid sequence of a fusion protein comprising a fragment of βhCG (amino acids 22-165) linked to a β-gal fragment while SEQ ID NO: 4 is a fusion protein comprising a fragment of βhCG (amino acids 22-165) linked to the FLAG peptide, the βhCG fusion protein of SEQ ID NO: 2 and SEQ ID NO: 4 differ with respect to their structure and physiochemical properties. A prior art search also requires a literature search. It is a burden to search more than one invention. Therefore, the

requirement of Group III and Groups I-II and IV-XVIII is still deemed proper and is therefore made FINAL.

3. Claims 11, 13-58 are withdrawn from further consideration by the examiner, 37 C.F.R. 1.142(b) as being drawn to non-elected inventions.

4. Claims 1-10 and 12 drawn to a composition comprising a recombinant β human chorionic gonadotropin fusion protein wherein the recombinant fusion protein consisting of βhCG protein, fragment or analog joined to a β-galactosidase protein of SEQ ID NO: 2 or fragment thereof, chitosan-based adjuvant are being acted upon in this Office Action.

5. Claim 1 is objected to because it is drawn to composition comprising β human chorionic gonadotropin protein (βhCG), fragments or analogs thereof and a chitosan-based adjuvant, which is a non-elected invention.

6. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: (1) The recitation of "βhCG ranges from about 10 μg to about 500 μg" in original claim 1 and (2) the recitation of "βhCG is about 25 μg" in original claim 2, (3) the recitation of "βhCG is about 250 μg" in original claim 3 and (4) "consisting essentially of" in original claim 12 have no support in the specification as filed. It is suggested that Applicants amend the specification to provide proper antecedent basis for the claimed subject matter.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-10 and 12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling only for (1) a composition comprising a recombinant fusion polypeptide comprising β human chorionic gonadotropin protein (βhCG) fused to β-galactosidase protein of SEQ ID NO: 2 and a chitosan-based adjuvant wherein he amount of βhCG ranges from about 10

μg to about 500 μg, (2) the said composition wherein the amount of βhCG is about 25 or 250 μg, (3) the said composition wherein the chitosan-based adjuvant comprises an emulsion of chitosan, sodium hydroxide, a biodegradable oil, a surfactant, and an aqueous buffer, (4) the said composition wherein the biodegradable oil is squalene, (5) the said composition wherein the ratio of βhCG fusion polypeptide to adjuvant is in the range of about 1:20 (w/w) to about 1:1500 (w/w), (6) the said composition wherein the adjuvant comprises chitosan, a metal salt, and an aqueous buffer, (7) the said composition wherein the metal salt is selected from the group consisting of zinc acetate, nickel sulfate, and copper sulfate, and (8) the composition wherein the recombinant polypeptide comprises a fusion protein consisting of a βhCG protein joined to a β-galactosidase protein for induction of infertility, **does not** reasonably provide enablement for (1) *any* composition comprising *any* "β human chorionic gonadotropin protein (βhCG)" and/or *any* "fusions", *any* "fragments" or *any* "analogs thereof", and a chitosan-based adjuvant, wherein the amount of *any* βhCG ranges from about 10 μg to about 500 μg, (2) *any* composition comprising *any* "β human chorionic gonadotropin protein (βhCG)" and/or any "fusions", *any* "fragments" or *any* "analogs thereof", and a chitosan-based adjuvant, wherein the amount of *any* βhCG ranges from about 10 μg to about 500 μg wherein the amount of βhCG is about 25 or 250 μg, (3) *any* composition mentioned above wherein the human chorionic gonadotropin protein comprises *any* "recombinant polypeptide", (4) *any* composition mentioned above wherein the human chorionic gonadotropin protein comprises *any* recombinant polypeptide wherein the recombinant polypeptide "further comprises" the amino acid sequence of SEQ ID NO: 2, (5) *any* composition comprising *any* β human chorionic gonadotropin protein (βhCG) and/or *any* fusions, *any* fragments or *any* analogs thereof, and a chitosan-based adjuvant, wherein the amount of *any* βhCG ranges from about 10 μg to about 500 μg wherein the chitosan-based adjuvant comprises an emulsion of chitosan, sodium hydroxide, a biodegradable oil, a surfactant, and an aqueous buffer, (6) *any* composition comprising *any* β human chorionic gonadotropin protein (βhCG) and/or *any* fusions, *any* fragments or *any* analogs thereof, and a chitosan-based adjuvant, wherein the amount of *any* βhCG ranges from about 10 μg to about 500 μg wherein the chitosan-based adjuvant comprises an emulsion of chitosan, sodium hydroxide, a biodegradable oil, a surfactant, and an aqueous buffer wherein the biodegradable oil is squalene, (7) the composition mentioned above wherein the ratio of *any* βhCG protein and/or *any* fusions, *any* fragments or *any* analogs thereof to adjuvant is in the range of about 1:20 (w/w) to about 1:1500 (w/w), (8) *any*

composition comprising *any* β human chorionic gonadotropin protein (βhCG) and/or *any* fusions, *any* fragments or *any* analogs thereof, and a chitosan-based adjuvant, wherein the amount of *any* βhCG ranges from about 10 μg to about 500 μg wherein the adjuvant comprises chitosan, *any* metal salt and *any* aqueous buffer, (9) *any* composition mentioned above wherein the metal is the ones such as recited in claim 10, (10) *any* composition mentioned above wherein the recombinant βhCG comprises *any* fusion protein consisting of "essentially" of *any* βhCG protein or *any* fragment or *any* analog thereof joined to β-galactosidase protein or *any* "fragment thereof" for induction of infertility. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The specification discloses only two recombinant βhCG polypeptides comprising SEQ ID NO: 2 and 4. The specification further discloses that the recombinant polypeptide of SEQ ID NO: 2 is a fusion protein consisting of β human chorionic gonadotropin protein fused to a β-galactosidase (page 14) while the recombinant polypeptide of SEQ ID NO: 4 is a fusion protein consisting of β human chorionic gonadotropin protein fused to a FLAG peptide (page 15). The βhCG fusion proteins mentioned above are made recombinantly and they are useful for inducing infertility.

The specification does not teach how to make and use *any* composition mentioned above comprising *any* "βhCG", *any* fusions, *any* fragments and *any* analogs thereof for inducing infertility because a fusion protein or a fusions, a fragment or an analog or recombinant polypeptide without SEQ ID NO has no structure, much less function. There is insufficient guidance as to which undisclosed composition comprising said undisclosed βhCG, fragment and analogs thereof fused to any undisclosed protein and recombinant polypeptide would have the same structure as the full-length βhCG polypeptide, let alone having the same function such as

inducing infertility. Further, there is insufficient in vivo working demonstrating that any undisclosed compositions mentioned above are effective for inducing infertility or uses as a contraceptive.

Ngo *et al* teach that the amino acid positions within the polypeptide/protein that can tolerate change such as conservative substitution or no substitution, addition or deletion which are critical to maintain the protein's structure/function will require guidance (see Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495).

Kuby *et al* teach that antibody epitopes (B cell epitopes) are not linear and are comprised of complex three-dimensional array of scattered residues which will fold into specific conformation that contribute to binding (See Kuby 1994, page 94, in particular). Immunization with a peptide fragment derived from a full-length polypeptide may result in **antibody specificity** that differs from the antibody specificity directed against the native full-length polypeptide. Without the specific amino acid residues, it is unpredictable that immunizing any fusion protein will generate antibody that specifically binds to the βhCG, in turn, would be useful for inducing infertility.

Abaza *et al* teach that even a single amino acid substitution outside the antigenic site can exert drastic effects on the reactivity of a protein with monoclonal antibody (the binding specificity of the antibody) against the site (See abstract, in particular). Given the indefinite number of undisclosed composition mentioned above, it is unpredictable which undisclosed composition comprising which undisclosed fusion protein such as any βhCG, any βhCG fragment, any analog thereof fused to any fragment of any β-galactosidase, and *any* recombinant polypeptide would be useful as a composition for inducing infertility. Since the fusion protein is not enabled, it follows that any composition comprising any fusion protein, any analog or fragment thereof wherein the amount of fusion protein ranges from about 10 to about 500 μg is not enabled. It also follows that the composition comprising any fusion protein, and a chitosan-based adjuvant, metal salt such as zinc acetate, nickel sulfate, and copper sulfate, and aqueous buffer is not enabled.

In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of

the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

9. Claims 1-10 and 12 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification does not reasonably provide a **written description** of (1) *any* composition comprising *any* "β human chorionic gonadotropin protein (βhCG)" and/or any "fusions", *any* "fragments" or *any* "analogs thereof", and a chitosan-based adjuvant, wherein the amount of *any* βhCG ranges from about 10 μg to about 500 μg, (2) *any* composition comprising *any* "β human chorionic gonadotropin protein (βhCG)" and/or any "fusions", *any* "fragments" or *any* "analogs thereof", and a chitosan-based adjuvant, wherein the amount of *any* βhCG ranges from about 10 μg to about 500 μg wherein the amount of βhCG is about 25 or 250 μg, (3) *any* composition mentioned above wherein the human chorionic gonadotropin protein comprises *any* "recombinant polypeptide", (4) *any* composition mentioned above wherein the human chorionic gonadotropin protein comprises *any* recombinant polypeptide wherein the recombinant polypeptide "further comprises" the amino acid sequence of SEQ ID NO: 2, (5) *any* composition comprising *any* β human chorionic gonadotropin protein (βhCG) and/or *any* fusions, *any* fragments or *any* analogs thereof, and a chitosan-based adjuvant, wherein the amount of *any* βhCG ranges from about 10 μg to about 500 μg wherein the chitosan-based adjuvant comprises an emulsion of chitosan, sodium hydroxide, a biodegradable oil, a surfactant, and an aqueous buffer, (6) *any* composition comprising *any* β human chorionic gonadotropin protein (βhCG) and/or *any* fusions, *any* fragments or *any* analogs thereof, and a chitosan-based adjuvant, wherein the amount of *any* βhCG ranges from about 10 μg to about 500 μg wherein the chitosan-based adjuvant comprises an emulsion of chitosan, sodium hydroxide, a biodegradable oil, a surfactant, and an aqueous buffer wherein the biodegradable oil is squalene, (7) the composition mentioned above wherein the ratio of *any* βhCG protein and/or *any* fusions, *any* fragments or *any* analogs thereof to adjuvant is in the range of about 1:20 (w/w) to about 1:1500 (w/w), (8) *any* composition comprising *any* β human chorionic gonadotropin protein (βhCG) and/or *any* fusions, *any* fragments or *any* analogs thereof, and a chitosan-based adjuvant, wherein the amount of *any* βhCG ranges from about 10 μg to about 500 μg wherein the adjuvant comprises chitosan, *any*

metal salt and *any* aqueous buffer, (9) *any* composition mentioned above wherein the metal is the ones such as recited in claim 10, (10) *any* composition mentioned above wherein the recombinant βhCG comprises *any* fusion protein consisting of "essentially" of *any* βhCG protein or *any* fragment or *any* analog thereof joined to β-galactosidase protein or *any* "fragment thereof" for induction of infertility.

The specification discloses only two recombinant βhCG polypeptides comprising SEQ ID NO: 2 and 4. The specification further discloses that the recombinant polypeptide of SEQ ID NO: 2 is a fusion protein consisting of β human chorionic gonadotropin protein fused to a β-galactosidase (page 14) while the recombinant polypeptide of SEQ ID NO: 4 is a fusion protein consisting of β human chorionic gonadotropin protein fused to a FLAG peptide (page 15). The βhCG fusion proteins mentioned above are made recombinantly and they are useful for inducing infertility.

With the exception of the specific fusion polypeptides of SEQ ID NO: 2 and 4, there is insufficient written description about the structure associated with function of *any* composition comprising *any* fusion protein, *any* fragment and analogs thereof, *any* βhCG, *any* βhCG fragment and analog thereof, joined to *any* β-galactosidase and fragment thereof and any recombinant polypeptide for a composition for inducing infertility.

The specification discloses only two fusion proteins of SEQ ID NO: 2 and 4 comprising only human hCG joined to β-galactosidase protein or FLAG peptide. Given the lack of a written description of *any* additional representative species of fusion protein, fragment and analog thereof, βhCG from other species, βhCG fragment and analog thereof, and recombinant polypeptide as encompassed by the claims, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.*

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

11. Claims 1-10 and 12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation of "fragments or analogs thereof" in claims 1 and 8 is ambiguous and indefinite because it is not clear whether the fragments or analogs thereof are referred to the fusion proteins or the βhCG alone or both fusion protein and βhCG. Appropriate correction is required.

The recitation of "the amount of βhCG is about 250 μg" in claim 3 has no antecedent basis in base claim 2. Claim 3 should depend on claim 1.

The recitation of "recombinant polypeptide" in claim 4 is ambiguous and indefinite because β human chorionic gonadotropin protein does not comprise a "recombinant polypeptide". It is the fusion protein, which is the recombinant polypeptide that comprises the β human chorionic gonadotropin protein.

The recitation of "further comprises" in claim 5 is ambiguous and indefinite because the recombinant polypeptide is the amino acid sequence of SEQ ID NO: 2.

The recitation of "recombinant βhCG" has no antecedent basis in base claim 4 because base claim 4 requires a recombinant polypeptide.

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 103(a) that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. This application currently names joint inventors. In considering Patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 1-4 and 6-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 91/16922 publication (Nov 1991, PTO 892) in view of EP 0368253 A2 (May 1990; PTO 1449) and Jones *et al* (The Lancet: 1295-1298; PTO 1449).

The WO 91/16922 publication teaches a composition (see page 25, lines 19-37, in particular) comprising various analog of β human chorionic gonadotropin (βhGC) fusion protein (chimera) such as hCG-beta/VSV-G fusion protein (full length beta subunit of human CG or fragment of hCG 39-56 (see page 13, line 7, in particular) fused to VSV-G or bovine LH (See page 10, line 6, Tables IV and XII, page 20, lines 7-13, page 23, line 10-18, in particular) in suitable vaccine adjuvant and suitable carriers, as known in the art (page 20, line 32-35, in particular). The reference β human chorionic gonadotropin (βhGC) fusion protein is a recombinant polypeptide (See pages 26, 42, Example 9, in particular).

The claimed invention in claim 1 differs from the reference only that the composition comprising a chitosan-based adjuvant, and the amount of (βhGC) ranges from about 10 μg to about 500 μg.

The claimed invention in claim 2 differs from the reference only that the amount of (βhGC) is about 25 μg.

The claimed invention in claim 3 differs from the reference only that the amount of (βhGC) is about 250 μg.

The claimed invention in claim 7 differs from the reference only that the biodegradable oil is squalene.

The claimed invention in claim 8 differs from the reference only that the ratio of βhGC fusion protein or analogs thereof to adjuvant is in the range of about 1:20 (w/w) to about 1: 500 (w/w).

The EP 0368253 A2 patent teaches chitosan-based adjuvant and a method of making said chitosan-based adjuvant for delivering any pharmaceutical such as human chorionic gonadotropin (See column 10, line 37, in particular) to a desired topical site of a test subject (See entire document, column 2, line 33-37, claims 1-10 of EP 0368253 A2, in particular). The EP 0368253 A2 patent teaches the chitosan-based adjuvant comprises an emulsion of chitosan, sodium hydroxide (See column 5, line 44-45, in particular), biodegradable oil such as eucalyptus oil, surfactant such as sodium lauryl sulfate or sorbitan and an aqueous buffer such as water (See column 11, line 10 bridging column 12, lines 1-30, in particular). The EP 0368253 A2 patent teaches the concentration of active ingredient to chitosan based delivery system can vary from as

little as 0.0001 up to 5 percent or higher by weight of the chitosan-based adjuvant (column 11, liens 36-39, in particular) which is in the range of 1:20 (w/w) or 5% to about 1:500 (w/w) or 0.2%.

Jones *et al* teach a contraceptive vaccine composition comprising a human βhGC fragment such as hCG-β CT peptide 109-145 conjugate to a carrier protein such as diphtheria toxoid in synthetic adjuvant such as N-acetyl-glcosamine-3yl-acetyl-L-alanyl-D-isogluamine (CGP-11637), and saline-oil emulsion vehicle with oil phase consisting of the biodegradable oil squalene and surfactant such as mono-oleate as emulsifying agent (See page 1296, column 1, in particular). Jones *et al* teach the amount of βhGC ranges from 50 μg to 1000 μg (See Table 1, page 1296, in particular). Jones et al teach the formulation is safe and efficacious in laboratory animals' study and appears to be suitable for use in man (See page 1296, first paragraph, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the adjuvant as known in the art as taught by the WO 91/16922 publication for the chitosan-based adjuvant as taught by the EP 0368253 A2 using the vaccine formulation as taught by Jones et al for a composition comprising β human chorionic gonadotropin (βhGC) fusion protein or analog thereof and a chitosan-based adjuvant, wherein the amount of βhGC ranges from about 10 μg to 1500 μg as taught by The WO 91/16922 publication, the EP 0368253 A2 patent and Jones *et al.* From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because the EP 0368253 A2 patent teaches chitosan-based adjuvant is useful for delivering any pharmaceutical such as human chorionic gonadotropin (See column 10, line 37, in particular). Jones *et al* teach the amount of βhGC ranges from 50 μg to 1000 μg (See Table 1, page 1296, in particular) is safe and efficacious in laboratory animal study and appears to be suitable for use in man (See page 1296, first paragraph, in particular).

In re Kerkhoven, 205USPQ 1069 (CCPA 1980), recognized that "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose ... [T]he idea of combining them flows logically from their having being individually taught in the prior art" (see MPEP 2144.06). The term "about" in claim 8 expands the claimed range of the analog

to the adjuvant to read on the reference range as taught by he EP 0368253 A2 patent (see column 11, liens 36-39, in particular), which is in the range of 1:20 (w/w) or 5% to about 1:500 (w/w) or 0.2%.

15. Claims 9-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 91/16922 publication (Nov 1991, PTO 892) in view of EP 0368253 A2 (May 1990; PTO 1449) and Jones *et al* (The Lancet : 1295-1298; PTO 1449) as applied to claims 1-4 and 6-8 mentioned above and further in view of US Pat No. 5,912,000 (June 1999, PTO 1449).

The teachings of the WO 91/16922 publication, the EP 0368253 A2 patent and Jones *et al* have been discussed supra.

The claimed invention in claim 9 differs from the references only that the composition wherein the adjuvant comprises chitosan, a metal salt, and an aqueous buffer.

The claimed invention in claim 10 differs from the references only that the metal salt is selected from the group consisting of zinc acetate, nickel sulfate, and copper sulfate.

The 5,912,000 patent teaches adjuvant such as chitosan for potentiating an immune response to any immunogen (See entire document, abstract, in particular). The reference chitosan comprises chitosan, a chelated metal ion such as copper, nickel or zinc from copper sulfate, nickel sulfate and zinc acetate (See column 4, Summary of Invention, lines 62-65, column 16, line 33-34, in particular) and an aqueous buffer such as PBS.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the chitosan based adjuvant as taught by the EP 0368253 A2 patent for the chitosan adjuvant comprising chitosan, a metal salt such as copper, nickel or zinc, and an aqueous buffer for a composition comprising β human chorionic gonadotropin (βhGC) fusion protein or analog thereof and a chitosan adjuvant comprising chitosan, a metal salt such as copper, nickel or zinc, and an aqueous buffer, wherein the amount of βhGC ranges from about 10 μg to 1500 μg as taught by The WO 91/16922 publication, the EP 0368253 A2 patent and Jones *et al.* From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because the 5,912,000 patent teaches adjuvant such as chitosan for potentiating an immune response to any immunogen (See entire document, abstract, in particular).

16. Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over WO 91/16922 publication (Nov 1991, PTO 892) in view of EP 0368253 A2 (May 1990; PTO 1449) and Jones *et al* (The Lancet : 1295-1298; PTO 1449) as applied to claims 1-4 and 6-8 mentioned above and further in view of US 5,602,005 (Feb 1997, PTO 892).

The teachings of the WO 91/16922 publication, the EP 0368253 A2 patent and Jones *et al* have been discussed supra.

The claimed invention in claim 9 differs from the references only that the recombinant βhGC comprises a fusion protein consisting essentially of a βhGC protein or fragment or analog thereof joined to a β-galactosidase protein or fragment thereof.

The '005 patent teaches a recombinant fusion protein consisting of SP-10 protein joined to a β-galactosidase protein or fragment thereof (See column 19, line 32-52, in particular) for use in a contraceptive vaccine. The '005 patent teaches the advantage of β-galactosidase protein slow down the degradation of the fusion protein during production and that the bacterial protein also functions as an adjuvant to enhance the immune response of the host to the recombinant fusion protein (See column 19, line 32-52, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the VSV-G in the hCG-beta/VSV-G fusion protein as taught by the WO 91/16922 publication for the β-galactosidase protein or fragment thereof in the fusion protein as taught by the '005 patent for a recombinant βhGC polypeptide comprises a fusion protein consisting essentially of a βhGC protein or fragment or analog thereof joined to a β-galactosidase protein or fragment thereof as taught by the WO 91/16922 publication and the '005 patent. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because the '005 patent teaches the advantage of β-galactosidase fusion protein slow the degradation of the fusion protein during production in addition to functions as an adjuvant to enhance the immune response of the host to the recombinant protein (See column 19, line 32-52, in particular).

17. No claim is allowed.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to "Neon" Phuong Huynh whose telephone number is (703) 308-4844. The examiner can normally be reached Monday through Friday from 9:00 am to 6:00 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

19. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401.

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